

‘Priming’ the brain to generate rapid upper-limb reactions

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Abstract Evoked autonomic nervous system (ANS) activity may be an important modulator of rapid reactions, generated in the face of urgency and may serve to augment the parallel somatosensory processing to adjust speed of processing. The primary objective of the current study was to temporally pair auditory stimuli with whole body perturbations to determine if conditioning could ‘prime’ the central nervous system (CNS) to respond faster and with greater ANS reactivity to the auditory stimulus alone. Healthy young participants ($n = 19$) were seated in a custom chair, which tilted backwards upon the release of an electromagnet and were instructed to reach to grasp a handle located in front of their arm as fast as possible following an auditory cue. Three conditions were completed in the following order: (1) *baseline*—auditory cue alone (5 trials); (2) *paired*—auditory cue, followed by a chair tilt 110 ms later (20 trials); and (3) *post-pairing*—auditory cue alone

(5 trials). Participants were not informed of the switch from paired to auditory-only stimuli in the first trial of the post-pairing task condition. Reaction time was measured using electromyography, and autonomic nervous system activity was monitored via the electrodermal response (EDR). The first trial *post-pairing* had significantly faster reaction time ($\Delta = 21$ ms) and significantly greater EDR amplitude compared to the last trial prior to pairing (baseline). The amplitude of contraction and overall time to handle contact were not significantly different between the first trial post-pairing and the last trial prior to pairing. This study demonstrates that the CNS can be ‘primed’ to generate rapid reactions and an elevated autonomic response in the absence of whole body instability. This indicates that afferent volume generated following whole body instability is not the only determinant of rapid reactions and emphasizes the importance of physiologic measures of autonomic activity with respect to stimulus-evoked reaction time.

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Introduction

‘Temporally urgent’ reactions are those that protect individuals from harm, such as balance recovery (Luchies et al. 2002; McIlroy and Maki 1993) and obstacle avoidance (Zettel et al. 2002), or are essential for skilled behavior, such as rapid stimulus-evoked reactions during skilled activity (Houlston and Lowes 1993; Land and McLeod 2000). In situations where urgent responses are essential, individuals with neurologic impairments tend to be slow to react, resulting in an increased risk of injury (Lakhani et al. 2011a; Marigold and Eng 2006;

McIlroy and Maki 1996). Despite the importance of speed of processing, there is currently a limited understanding of the mechanisms that control this class of temporally urgent reactions. While some rapid stimulus-evoked reactions may be characterized by processing via ‘reflexive pathways’ to autogenic or startling stimuli (Chokroverty et al. 1992; Valls-Solé et al. 1995), many of the rapid behaviors are learned and do not simply reflect reflexive networks (Lakhani et al. 2011b; McIlroy and Maki 1995; Tripp et al. 2004). For example, the complexity of reach-to-grasp behaviors in response to postural instability features extremely rapid responses that are elegantly matched to the surrounding environment (Gage et al. 2007). The challenges of such control, which require complex integration of extero- and interoceptive stimuli following stimulus onset, are not easily accounted for by simple central nervous system (CNS) networks. What is not clear is the mechanism by which the CNS is capable of these rapid processing times for such complex behavior in response to sensory stimuli. The current work seeks to extend our understanding of the capacity of the CNS to rapidly process information. Arguably, the literature to date has been informed by ‘classic’ reaction times paradigms, which request that individuals react as ‘fast as possible’ to visual or auditory cues. So, while the responses are stimulus driven, they are not temporally urgent and therefore significantly understate the capacity for speed of processing within the CNS.

Currently, we employ a paradigm that utilizes the application of unpredictable whole body disturbances, such as standing/seated surface translations and seated chair tilts (Gage et al. 2007; Lakhani et al. 2011b; Sibley et al. 2008), as a cue to elicit rapid multi-joint movements. Previous work using this model has demonstrated significantly shorter response onset latencies (~100 ms) when compared to simple auditory or visual stimuli that cue comparable volitional movement patterns (~200 ms; i.e., a step or reach-to-grasp response) (Gage et al. 2007; Lakhani et al. 2011b; Sibley et al. 2010a). Furthermore, balance recovery movements alone do not appear to be a requirement for rapid reactions. Recently, we have demonstrated that stimulus–response congruence is not required in order to generate rapid reactions following a seated whole body disturbance (Lakhani et al. 2011b). For example, individuals reacted in less than 90 ms with both the appropriate balance recovery muscle group in a reach-to-grasp task (anterior deltoid) and an inappropriate balance recovery muscle group (medial gastrocnemius). This finding suggested that rapid reactions may be driven by characteristics of the stimulus, and, in particular, the magnitude of somatosensory afferent information generated by the high intensity of a whole body perturbation. Collectively, the work to date seems to lead to the hypothesis that the properties of the sensory stimuli (i.e., modality, amplitude) are critical to the generation of these extremely rapid reactions.

While it appears that stimulus characteristics may be the most important in the generation of rapid responses, it is also the case that such stimuli evoke phasic autonomic responses, as revealed by electrodermal responses (EDR) time locked to perturbations (Maki and Whitelaw 1993; Sibley et al. 2008; 2009). The EDR is used as psychophysiologic measure of preparation for impending action and records changes in sweat production, reflective of increased autonomic nervous system (ANS) activity (Boucsein et al. 2012; Critchley et al. 2000). Arousal has been frequently cited as a possible modulator of reaction time related to motivation, risk and reward of the task (Sibley et al. 2008, 2010b). Although causality has not been determined, previous work has highlighted the phasic responses of the ANS as reflected by electrodermal responses temporally coupled to whole body instability (Sibley et al. 2008, 2010a). Therefore, it is conceivable that rapid processing speeds arise from the concurrent autonomic activation from associated sensory inputs, rather than the direct influence of the sensory stimulus.

This study is designed to further probe the importance of stimulus properties and the associated autonomic responses on reaction time that are generated by whole body instability. The pairing of an auditory cue with a whole body-seated perturbation can be used to condition a rapid reach-to-grasp reaction to an auditory cue (Campbell et al. 2009). Specifically, if the rapid onset reactions associated with whole body instability can occur to a low-amplitude auditory tone, in the absence of whole body instability (initial post-conditioning trial), then this would support the view that perturbation-generated somatosensory input alone is not the primary determinant of reaction time. In this case, other state characteristics of the individual such as arousal and attention may be of equal or greater importance. In this regard, the presence of a phasic ANS response following conditioning, potentially linked to more rapid onset responses, may support the view that phasic ANS reaction plays a role in modulating response latency.

The primary objective of the current study was to determine whether the sensory stimulus (specifically that evoked by whole body instability) is a necessary requirement for initiating rapid upper-limb motor responses and evoked ANS responses or whether such responses can be conditioned to be triggered by a temporally unpredictable low-amplitude stimulus.

Experimental procedure

Participants

Nineteen healthy young adults (22 ± 3 years old; 13 female) participated in this study. This study was reviewed and approved by the Office of Research Ethics at the

University of Waterloo. All participants provided informed written consent. None of the participants had any neurologic or musculoskeletal disorders that may have affected their ability to complete the tasks.

Protocol

Participants were seated in a custom-designed chair that could tilt backwards upon the release of an electromagnetic (Fig. 1) and is described in further detail elsewhere (Lakhani et al. 2011b; Sibley et al. 2010b). A handhold was fixed in place approximately 30 cm in front of the participant's dominant upper limb, in-line with the acromion process. Participants were asked to reach to grasp the handle as fast as possible following the presentation of a low-amplitude auditory cue (60 db, 100 ms duration, 440 Hz) in three different conditions (Fig. 2), delivered in the following order: (1) *baseline*—auditory cue alone (5 trials), (2) *paired*—auditory cue followed by a chair tilt 110 ms later (20 trials), and (3) *post-paired*—auditory cue alone (5 trials). The delay of 110 ms between stimuli in the *paired* condition was selected in order to allow sufficient time for the auditory stimulus to generate cortical potentials in the frontal cortex, as has been previously demonstrated in studies of human auditory-evoked potentials (Picton et al. 1974), prior to the evocation of a secondary stimulus. The inter-trial intervals were randomized and lasted from 20 to 60 s. Trials were presented without breaks unless requested by the participant, and the experiment lasted 25–30 min once

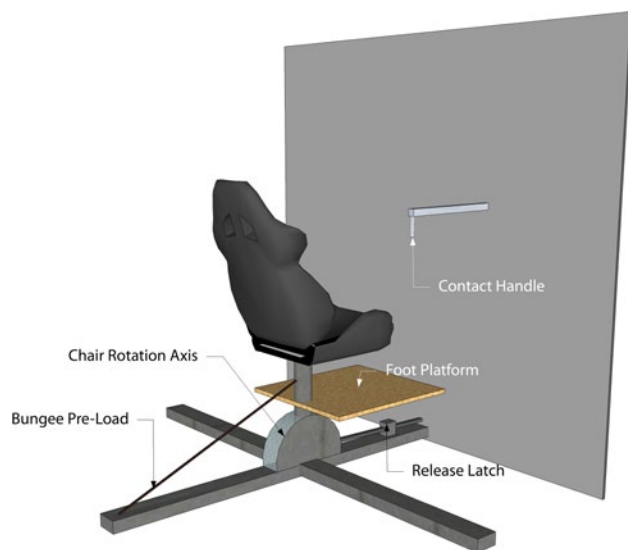


Fig. 1 Tilting-chair setup. Participants were seated in a custom-designed chair and in received either a 60 db auditory stimulus alone (*baseline* and *post-pairing* trials) or a 60 db tone, followed 110 ms later by a transient posterior whole body perturbation (*paired* trials). In all conditions, participants were instructed to reach and grasp the handle as fast as possible following the auditory stimulus

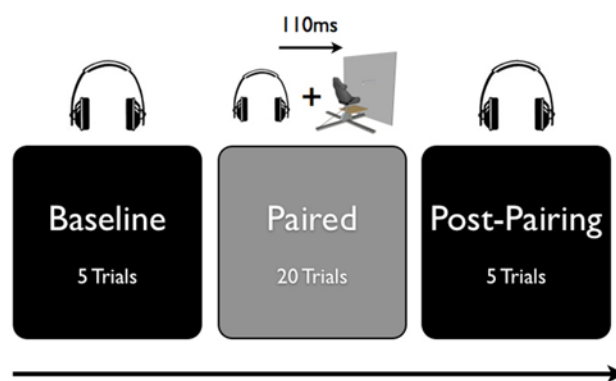


Fig. 2 Summary of protocol task conditions. In all conditions, participants were to reach and grasp a handle as fast as possible in response to the auditory tone. *Baseline* five trials where only the tone was presented, *paired* twenty trials where the tone was presented, followed 110 ms later by a chair tilt. *Post-pairing* the tone was again presented alone. Participants were not informed that there would be no chair tilt

underway. Participants were not informed that the first trial following the series of *paired* trials would be auditory alone.

Measures

Electromyography (EMG) was collected from the anterior deltoid (AD) and flexor digitorum superficialis (FDS) of the dominant upper limb. EMG sites were cleaned with alcohol and abrasive cream and shaved if necessary. Silver/silver chloride electrodes were fixed 1 cm apart over each muscle belly. EMG signals were amplified by a magnitude of 1,000 (Bortec Biomedical, Calgary, AB) and stored for offline processing.

EDR was measured using two electrodes placed on the middle phalanges of the second and third digits of the participant's non-dominant hand (SCA1 Skin Conductance Adaptor, Grass Technologies, West Warwick RI). Electrode sites were cleaned with rubbing alcohol, and the electrodes were filled with isoelectric paste. The signal was pre-amplified at a gain of 5, low pass filtered online at 10 Hz and stored for offline analysis.

A load cell, embedded in parallel with the electromagnetic release of the chair was used to indicate perturbation onset time. All signals were collected at a frequency of 1,000 Hz.

Signal processing

Auditory stimulus onset time was noted by a 5 V square wave that was recorded when an auditory stimulus was delivered. In trials that included a perturbation, perturbation onset time was determined to be the time at which the load on the electromagnetic chair latch was less than 5 N.

In all conditions, motor onset latency (reaction time) was determined relative to the auditory tone onset.

EMG signals were digitally filtered from 20 to 250 Hz (second-order dual pass Butterworth) and conditioned by removing any DC offset bias and by full wave rectifying the signal. Reaction time was determined by the onset of EMG activity, which was defined as the time when the EMG amplitude exceeded five standard deviations of the mean of a 100 ms baseline value taken prior to the auditory stimulus delivery. Movement time was defined as the time between the onset of the auditory tone and the time of contact with force sensing resistors located around the hand-hold. Integrated EMG (iEMG) amplitude was normalized relative to the mean of the iEMG amplitude 100 ms following the onset for the baseline condition for each individual muscle (i.e., the baseline condition amplitude was set at 100 % for each muscle, and the amplitudes from the other conditions were compared relative to baseline). The baseline iEMG amplitude was recorded to indicate if the participant was contracting prior to the onset of the stimulus and was the average normalized amplitude, as a percentage of the participant's average muscle activity in the baseline condition, for one second prior to the onset of the auditory stimulation.

EDR recordings were filtered with a second-order low pass filter at 5 Hz. The phasic EDR onset latency was defined as the time when a positive, sustained increase in slope, greater than 5 standard deviations from the baseline EDR 100 ms prior to stimulus onset, occurred between 0.5 and 5 s following perturbation onset. Integrated EDR (iEDR) amplitude was the integrated sum of the area under the EDR response curve for the first 5 sec following phasic EDR onset.

Statistical analysis

Pearson's correlation analysis was conducted to establish any significant relationships between outcome measures. The primary analysis focused on the outcome measures for auditory-only-evoked reactions to determine the influence of pairing. A paired *t* test was done between the last trial

prior to conditioning (baseline) and the first trial following conditioning (post-pairing). Contrast analyses using a one-way Analysis of Variance (ANOVA) were conducted between the first trial post-pairing and the subsequent trials post-pairing to explore the extinction the conditioning effect. The secondary analysis focused on the mean differences between auditory-evoked and perturbation-evoked response characteristics at three different time points (baseline, paired, and first trial post-pairing). A one-way repeated measures ANOVA was used to make such comparisons. Pairwise comparisons were conducted using a Tukey post hoc test to compare outcome measures relative to the baseline condition.

Consistent with previous work (Lakhani et al. 2011b), there was a rapid adaptation following the presentation of the very first trial in the baseline condition, which was triggered with an auditory stimulus alone. In this case, the first trial in the baseline condition demonstrated a significantly greater onset latency (AD: $F_{1,72} = 71.00$, $p < 0.0001$; FDS: $F_{1,72} = 53.51$, $p < 0.0001$) and a significantly greater movement time ($F_{1,72} = 24.20$, $p < 0.0001$) compared to the average of the four following baseline trials. Due to this rapid adaptive change, statistical analyses do not include the first baseline trial.

Results

All participants successfully completed all trials in all conditions. Results are summarized in Table 1. Note that electrodermal skin response data and movement time were unavailable for one participant due to technical difficulty. Representative EMG traces for a single trial from the baseline and first trial post-pairing are displayed in Fig. 3. Results were analyzed with a focus on a series of a priori comparisons. The primary analyses were conducted on the influence of the pairing condition on auditory-evoked responses and on the extinction of that adaptation in the subsequent trials after the paired stimulus task condition. The subsequent analysis was conducted on the primary

Table 1 Summary of response characteristics across the three conditions (mean $\pm$ standard error)

	Baseline (first trial)	Baseline (subsequent trials)	Paired	Post-pairing (first trial)	Post-pairing (subsequent trials)
Anterior deltoid onset (ms)	265 $\pm$ 19	181 $\pm$ 5.5	157 $\pm$ 4	162 $\pm$ 6	187 $\pm$ 10
Flexor digitorum superficialis onset (ms)	294 $\pm$ 24	210 $\pm$ 11	177 $\pm$ 6	224 $\pm$ 33	215 $\pm$ 12
Anterior deltoid iEMG	108 %	93 %	387 %	127 %	102 %
Flexor digitorum superficialis iEMG	109 %	95 %	338 %	156 %	92 %
EDR onset (s)	2.15 $\pm$ 0.10	2.03 $\pm$ 0.06	1.90 $\pm$ 0.05	1.99 $\pm$ 0.08	2.02 $\pm$ 0.06
iEDR (μ mhos $\cdot$ ms)	4,301 $\pm$ 862	4,326 $\pm$ 850	6,486 $\pm$ 926	5,695 $\pm$ 943	3,958 $\pm$ 613
Movement time (ms)	617 $\pm$ 31	507 $\pm$ 17	409 $\pm$ 7	491 $\pm$ 54	511 $\pm$ 25

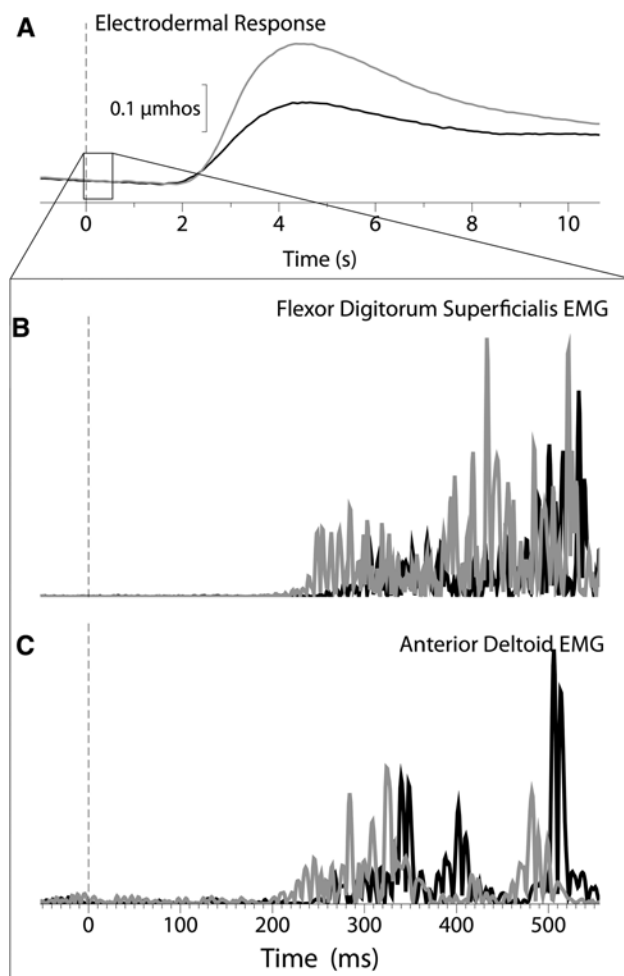


Fig. 3 Electrodermal Response (a), Flexor Digitorum Superficialis EMG (b) and Anterior Deltoid EMG (c) for a single trial from a representative participant, comparing a representative *baseline* trial (black) and the *first trial post-pairing* (gray). The dashed vertical line denotes auditory stimulus onset

differences in the task in the paired and unpaired conditions (i.e., auditory only vs. auditory + perturbation responses).

Overall, there were statistically significant modest, negative correlations between the integrated EDR amplitude and the onset latency of the anterior deltoid and flexor digitorum superficialis muscles (Pearson's $r = -0.48709$, $p = 0.010$ and Pearson's $r = -0.50240$, $p = 0.0076$, respectively). Additionally, there was a statistically significant strong positive correlation between the integrated EDR amplitude and iEMG of the anterior deltoid (Pearson's $r = 0.78092$, $p < 0.0001$).

There were no significant differences of baseline AD and FDS EMG activity prior to stimulation between conditions ($F_{2,36} = 0.68$, $p = 0.5148$ and $F_{2,36} = 0.74$, $p = 0.4840$, respectively). In addition, in all conditions, pre-stimulus EMG activity accounted for a negligible percentage of the normalized average EMG activity for each

subject 100 ms following EMG onset in the baseline condition (AD: baseline = 0.03 %, pairing = 0.04 %, post-pairing = 0.04 %; FDS: baseline = 0.07 %, pairing = 0.05 %, post-pairing = 0.04 %).

Auditory-evoked responses: influence of pairing

Reaction and movement time

Note that comparisons between the first trial after post-pairing and the last trial prior to pairing were used as the index of the influence of conditioning and that both of these trials were evoked only by the same low-amplitude auditory tone. Paired t-tests demonstrated a significantly shorter AD onset latency in the first trial immediately after pairing when compared to the last trial before pairing (163 vs. 184 ms; $t_{18} = 3.18$, $p = 0.0052$; Fig. 4). There was, however, no significant difference in the FDS muscle onset latency (214 vs. 224 ms; $t_{18} = -0.36$, $p = 0.7214$). There was no significant difference in movement time between the first trial post-pairing and the last trial before pairing (510 vs. 491 ms; $t_{18} = 0.37$, $p = 0.7128$).

EMG amplitude

Consistent with the lack of difference in movement time, there was no significant difference in AD activation amplitude ($t_{18} = -1.57$, $p = 0.1335$) or FDS activation amplitude ($t_{18} = -1.05$, $p = 0.3064$) in the first trial post-pairing compared to the last trial prior to pairing.

Electrodermal response

There was no significant difference in the mean latency timing of the onset of the EDR relative to the stimulus onset between the last trial prior to pairing and first trial of the post-pairing ($t_{17} = -0.18$, $p = 0.8619$; Fig. 5). However, there was a significantly greater integrated EDR amplitude in the first trial post-pairing compared to the last trial prior to pairing ($t_{17} = -2.349$, $p = 0.0316$).

Auditory-evoked responses: extinction of pairing effect

Reaction and movement time

In this analysis, the first trial after pairing was compared to the subsequent trials after pairing. Overall, there was a non-statistically significant trend for AD onset latency ($F_{1,72} = 3.13$, $p = 0.0810$) and no statistically significant difference of FDS onset latency ($F_{1,72} = 0.15$, $p = 0.7006$). However, it should be noted that the mean onset latency of the AD in the subsequent trials post-pairing was 25 ms

Fig. 4 Reaction time by trial. Group mean $\pm$ standard error for each individual trial in the three task conditions (*B* baseline, *C* conditioning, *PP* post-pairing)

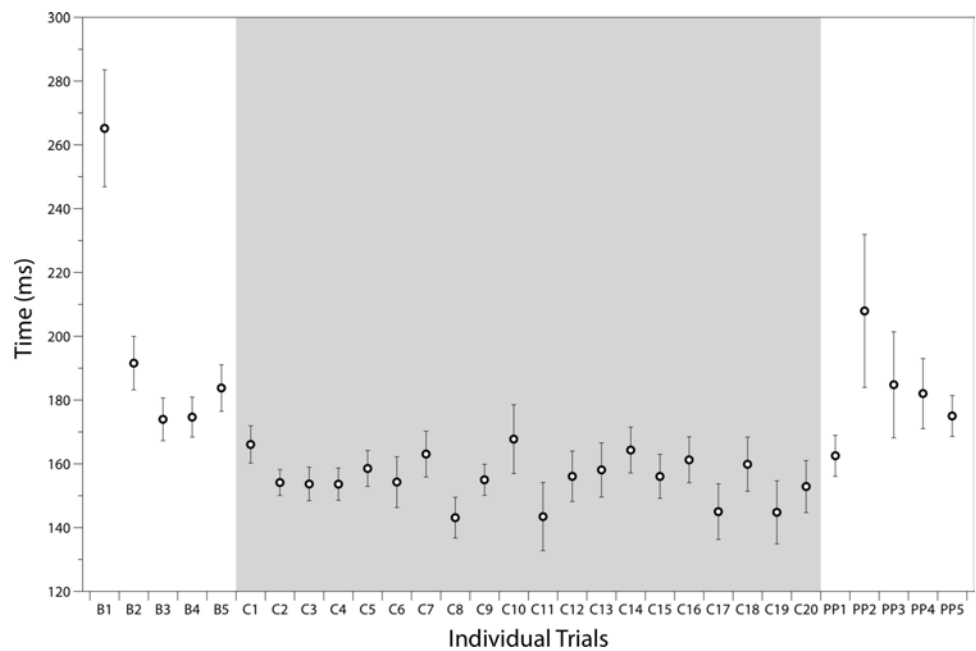
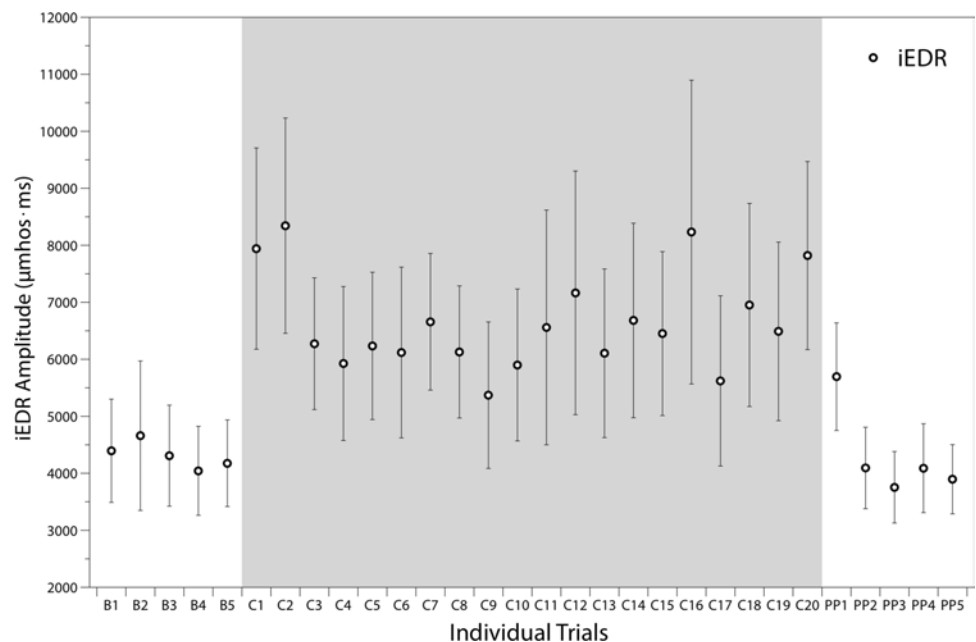


Fig. 5 Integrated EDR amplitude by trial. Group mean $\pm$ standard error for each individual trial in the three task conditions (*B* baseline, *C* conditioning, *PP* post-pairing)



slower than the initial post-pairing trial (187 vs. 162 ms). There was no statistically significant difference in movement time between the first trial post-pairing and the subsequent trials post-pairing (491 vs. 511 ms; $F_{1,68} = 0.08$, $p = 0.7811$).

EMG amplitude

There was a significantly greater iEMG amplitude in the first trial post-pairing for both the AD ($F_{1,72} = 4.10$,

$p = 0.0465$) and the FDS ($F_{1,72} = 6.52$, $p = 0.0128$) compared to the subsequent post-pairing trials.

Electrodermal response

There was a significantly greater integrated EDR amplitude ($F_{1,68} = 41.32$, $p < 0.0001$) in the first trial post-pairing compared to the subsequent trials post-pairing. There was, however, no significant difference in EDR onset latency ($F_{1,68} = 0.38$, $p = 0.5420$).

Task differences in response characteristics: paired versus unpaired

Reaction time and movement time

To determine the relationship between the conditioning state (auditory tone paired with perturbation) and the auditory-only-task conditions, comparisons across the tasks (baseline, paired, post-pairing: first trial) were conducted. Overall, across tasks, there was a significantly different muscle onset latency for the anterior deltoid ($F_{2,36} = 18.92$, $p < 0.0001$). Post hoc testing revealed that the anterior deltoid onset latency in the baseline condition was significantly slower than the paired & the first trial post-pairing conditions ($p < 0.05$), but that there was no significant difference between the paired response latencies and the first trial post-pairing (157 vs. 163 ms, respectively). Additionally, there was a statistically significant difference in FDS onset latency across the three task conditions ($F_{2,36} = 4.24$, $p = 0.0222$). Post hoc testing revealed that the FDS onset latency in the baseline condition was significantly greater than the paired condition ($p < 0.05$), but not different from the first trial post-pairing ($p > 0.05$). There was a significantly different movement time between the three conditions ($F_{2,36} = 8.83$, $p = 0.0008$). Post hoc analysis revealed a significant decrease in movement time in the paired condition compared to baseline ($p < 0.05$), and no significant difference between the baseline condition and the first trial post-pairing ($p > 0.05$).

EMG amplitude

There was a significantly different anterior deltoid iEMG amplitude between baseline, paired and the first trial post-pairing ($F_{2,36} = 52.58$, $p < 0.0001$). Post hoc testing revealed that the iEMG amplitude of the baseline condition was significantly smaller than in the paired condition ($p < 0.05$) and not significantly different from the first trial post-pairing ($p > 0.05$). Additionally, there was no significant difference between the FDS iEMG amplitude across the three task conditions ($F_{2,36} = 3.11$, $p = 0.0569$).

Electrodermal response

There were significant differences in iEDR amplitude ($F_{2,34} = 14.11$, $p < 0.0001$) and EDR onset latency ($F_{2,34} = 5.16$, $p = 0.0110$) between the three task conditions. Post hoc testing revealed a significantly greater iEDR amplitude in the paired condition compared to baseline ($p < 0.05$). With respect to EDR onset, there were no significant pairwise differences between any of the three conditions.

Discussion

The primary objective of this study was to understand whether stimulus properties of whole body instability are required in order to generate rapid reaction times, or whether it was possible to condition a low-amplitude auditory stimulus to evoke similarly rapid reactions. In addition, the study set out to further our understanding of the potential involvement of phasic autonomic activity in the generation of these responses.

Perturbation-generated somatosensory information is not a necessary requirement for rapid reaction times

This study demonstrated that the onset of upper-limb responses equivalent to those generated by whole body instability could be evoked with low-amplitude auditory stimuli (60 db tone). We have previously hypothesized that the large volume of somatosensory drive generated from a whole body-balance disturbance is a necessary requirement for rapid reaction times (Lakhani et al. 2011b, 2012). However, the current work demonstrated that the expected stimulus context (i.e., expectation of a balance disturbance) could initiate a rapid response, despite the timing of the stimulus remaining unpredictable. Central set has previously been implicated in the response preparation for whole body-balance disturbances as a modulator of sensorimotor processes (Mochizuki et al. 2008; Prochazka 1989). Cortical activity prior to temporally predictable perturbations has been well-documented by other investigators and is typically denoted using electroencephalography by a slow wave negativity 1.5–2 s prior to the perturbation (Saitou et al. 1996; Slobounov et al. 2005). In the current experiment, despite the consistent delivery of the auditory cue prior to the perturbation, it is unlikely that the participants were able to evoke a similar level of cortical anticipatory activity due to the lag between the auditory cue and perturbation (110 ms). However, the overall central set associated with the repetitive delivery of postural perturbations could have played an important role in preparing the CNS to generate a rapid response.

A number of models have been generated to theorize the build-up of neuronal activity in anticipation of an impending event until a threshold is reached and a decision is made (Bogacz and Gurney 2007; Reddi et al. 2003). Previous work has demonstrated that the rate of integration of neuronal activity is related to the motivation, risk, and reward associated with the upcoming task, and neurophysiologic studies have implicated the superior colliculus, lateral intraparietal area, and prefrontal cortex as the likely regions for the accumulation process (Munoz and Wurtz 1995; Reddi and Carpenter 2000; Roitman and Shadlen 2002). The LATER model (linear approach to threshold

with ergodic rate) attempts to quantify the time needed to make decisions based on the rate of rise of neuronal activity from stimulus to action, the baseline neuronal activity and the threshold required to generate a response (Reddi and Carpenter 2000). Empirical tests of the LATER model using saccades suggested that when more information was provided about an impending stimulus, the rate of rise to a threshold level was increased, whereas if the level of urgency to generate a response was higher, the threshold level was reduced altogether (Reddi et al. 2003). In the current study, participants were given information about the impending stimuli, though not specific details about the timing of the onset. They were also in a situation where an urgent response was required in order to maintain upright stability. Thus, the reduced reaction time could be the product of elevated pre-stimulus neuronal activity which acts to either alter the threshold or the rate of rise to a threshold in order to generate activity. Importantly, despite the lack of statistical significance, there was a trend toward slower reaction time in the AD in the subsequent trials post-pairing, indicating how the CNS may act to rapidly ‘reset’ in the absence of an impending whole body-balance disturbance.

Post-stimulus autonomic activity is related to the expectation of an urgency inducing stimulus

There are a number of studies indicating that the ANS likely assists in generating rapid responses to urgent stimuli, such as a balance disturbance; however, the underlying CNS mechanism is unknown (Sibley et al. 2008, 2009). In the current study, EDR was used as a proxy measure of ANS activity, demonstrating that in the first trial post-pairing, the amplitude of EDR activity was significantly greater than both the baseline condition and the subsequent post-pairing trials.

The reduced reaction time and elevated integrated EDR in the first trial following the *paired* condition indicates that the pairing between the auditory and perturbation stimuli was an adaptation, as is commonly observed in Pavlovian fear conditioning (Davis 2000; Ledoux 2000). Cheng et al. (2006) investigated amygdalar excitability, using functional magnetic resonance imaging and the EDR during the conditioning of fear responses in humans, demonstrating that significant amygdalar activity was only present when the conditioning stimulus, which predicted an electrical shock, resulted in a phasic EDR (Cheng et al. 2006). In situations where the conditioning stimulus did not result in an EDR, the amygdalar activity was minimal, indicating that the amygdala is likely not only involved in the acquisition of fear associations, but also in the physiologic expression of autonomic activity (Cheng et al. 2006). With respect to the current study, this indicates that the elevated EDR in the

first post-pairing trial was likely not simply the result of a learned association in the conditioning of the response, but also related to the level of amygdala activity generated by the auditory stimulus.

Previous work has also established that the EDR is a summation of both sensory inputs (i.e., a whole body-balance disturbance) and motor outputs (i.e., reaching to grasp a handle) and the amplitude of the EDR severely attenuated either the sensory or motor output which is not present in the response (Sibley et al. 2009). In the current study, we demonstrated that a large magnitude EDR can be temporarily evoked in the absence, but expectation, of the appropriate sensory input, indicating potential cognitive relationships to the EDR. In light of this, Sibley et al. (2010a, b) demonstrated dissociation between the level of cortical excitability and EDR following whole body-balance disturbances and concluded that although cortical and EDR response amplitudes are changed with the introduction of a perturbation, the variables may not be related (Sibley et al. 2010b). This is supported by Hajcak et al. (2003) who demonstrated that the EDR is related to error awareness (Hajcak et al. 2003), and in the current study, the EDR may have been elevated due to the unexpected absence of a perturbation following the auditory stimulus. As has been previously described, it is important to note that the long onset latency of the sweat response was used to generate the EDR results in the inability to draw conclusions regarding the temporal profile of the EDR with respect to the latency of the EMG onset. However, it appears that the EDR can be driven by the mere expectation of a temporally unpredictable stimulus, coupled with the initiation of the appropriate motor outflow.

Scaling of EMG response amplitude is related to stimulus properties

A number of perturbation studies have demonstrated that the amplitude of EMG activity (i.e., the 100 ms post-onset iEMG) at the primary agonist for a balance recovery response scales to the reaction time (Gage et al. 2007; Lakhani et al. 2011b; Sibley et al. 2010a). For example, a perturbation-evoked reach-to-grasp response will generate a significantly greater iEMG amplitude at the anterior deltoid and a faster reaction time than an auditory cued reach-to-grasp response, despite similar kinematic profiles (Gage et al. 2007; Lakhani et al. 2011b). In the current study, it was surprising that the first trial post-pairing condition did not display significantly greater iEMG amplitude at the anterior deltoid compared to the baseline, despite a reaction time that was 20 ms faster than baseline. Furthermore, the iEMG amplitude of the anterior deltoid during the *paired* condition was three times greater than the first trial post-pairing, despite these two conditions not having

significantly different reaction times at the anterior deltoid. This is an important distinction indicating that the onset of EMG activity and the amplitude of EMG activity may be independently controlled by the CNS. Specifically, the amplitude of EMG activity may not be determined by the anticipated stimulus, but rather, may be specifically determined by the characteristics of the afferent discharge associated with the stimulus.

In spite of the speed of movement, the evoked muscle response is likely comprised of at least two distinct phases. The initial onset phase of the EMG response, which generates defines reaction time, is at least influenced by pre-stimulus onset properties such as anticipated stimulus characteristics and learned associations while reflecting a limited reliance on the actual characteristics of the stimulus and their afferent input into the CNS. The later phase of the response, following the initial burst of activity, reflects ongoing afferent feedback regarding the actual stimulus properties, which once recognized by the CNS, might act to reduce the overall gain of the EMG response, also resulting in an overall movement time that was comparable with the baseline, despite the reduced reaction time in the first trial post-pairing. The discrimination between reaction time and EMG response amplitude is counter to hypotheses from our previous work (Gage et al. 2007; Lakhani et al. 2011b; Sibley et al. 2010a), which postulated that a generalized increase in CNS gain results in rapid reaction time coupled with large EMG amplitude. Because muscle activation of the responding limb typically occurs in a proximal to distal manner, the lack of an onset latency reduction in the FDS or in movement time following conditioning can be explained with respect to the distinct phases of the upper-limb movement. Conditioning appeared to only affect the earliest onset of muscle onset anywhere in the limb, rather than influencing the timing throughout the entire the movement. This may be the result on feedback provided to the CNS following the initial response, which indicated the absence of a whole body-balance disturbance.

Conclusions

The current study demonstrated that the afferent feedback generated from a whole body-balance disturbance is not required to generate rapid responses, revealing latencies that are not typically generated in the absence of a temporally urgent stimulus. Furthermore, this study demonstrates that the EDR generated in the absence of a balance disturbance can be temporarily manipulated by altering the context of a given stimulus and that the EMG response amplitude can be dissociated from the onset latency of the same muscle. These findings suggest that afferent somatosensory information generated following a stimulus may not be the

only important instigator of rapid peripheral responses and that conditioned associations, as well as available information regarding expected stimulus properties play critical roles in determining response characteristics.

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